

### **REMARKS**

Reconsideration of this application, as amended, is respectfully requested. Claims 1-13 were pending in this application. Claims 1-3 and 7 have been cancelled. Claims 4, 5, 12 and 13 have been amended without prejudice or disclaimer. Applicants reserve the right to prosecute any cancelled subject matter in a later filed divisional or continuation application. Claims 4-6 and 8-13 are currently pending. Consideration and entry of these documents is respectfully requested.

### **DOCKET NUMBER**

Applicants hereby request that the Attorney Docket No. for this application be changed from 1038-1026 MIS:jb to "API 1038-07-US".

### **DRAWINGS**

New drawings representing Figs. 1-19C are attached to this response. Applicants believe these corrected drawings are in compliance with USPTO regulations.

### **DOUBLE PATENTING**

Claims 1-3 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7 and 11 of U.S. Pat. No. 5,506,139. Claims 1-3 have been cancelled. The rejection is therefore moot.

Claims 1-3 also stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 7-12 of U.S. Pat. No. 6,147,057; claims 1-12 of U.S. Pat. No. 6,025,342; claims 1-12 of U.S. Pat. No. 5,981,503; claims 10, and 12-20 of U.S. Pat. No. 5,939,297; claims 11 and 13-22 of U.S. Pat. No. 5,869,302. Claims 1-3 have been cancelled. The rejection is therefore moot.

### **REJECTIONS UNDER 35 U.S.C. 112, FIRST PARAGRAPH (ENABLEMENT)**

#### **A. Claims 4, 12 and 13**

Claims 4, 12, and 13 stand rejected under 35 U.S.C. 112, first paragraph for lack of enablement. Applicants are in the process of making the required biological deposits.

Once the deposits are made, Applicants will amend the specification to insert the required information and provide the Examiner with copies of the deposit receipts.

**B. Claims 1, 5, 6, 9-11 and 14**

Claims 1, 5, 6, 9-11 and 14 stand rejected under 35 U.S.C. 112, first paragraph for lack of enablement. Applicants respectfully traverse these rejections as indicated below.

Claims 1 and 7 have been cancelled and, therefore, the rejections as to these claims are moot.

Claim 5 has been amended. Claims 9-11 and 14 are dependent upon claim 5. Accordingly, Applicants respectfully request that the rejection of claims 5, 9-11 and 14 be withdrawn.

**C. Claims 1, 2, 5, 6 and 7**

Claims 1, 2, 5, 6 and 7 stand rejected under 35 U.S.C. 112, first paragraph for lack of enablement. Applicants respectfully traverse these rejections as indicated below.

Claims 1, 2 and 7 have been cancelled and, therefore, the rejections as to these claims are moot.

Claim 5 has been amended. Claim 6 is dependent upon claim 5. Accordingly, Applicants respectfully request that the rejection of claims 5 and 6 be withdrawn.

**REJECTIONS UNDER 35 U.S.C. 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)**

Claims 4, 12, and 13 stand rejected under 35 U.S.C. 112, first paragraph for lack of written description. As mentioned above, Applicants are in the process of making deposits of the plasmids named in claims 4, 12 and 13. As the Examiner is aware, the Federal Circuit recently held that ATCC deposits may be used to satisfy the written description requirement. Applicants believe the instant case is one such instance.

**REJECTIONS UNDER 35 U.S.C. 102(b)**

Claims 1-3 stand rejected under 35 U.S.C. 102(b) or in the alternative 103(a) for being unpatentable in view of U.S. Pat. No. 5,506,139. Claims 1-3 have been cancelled and, therefore, the rejections are moot.

**REJECTIONS UNDER 35 U.S.C. 103(a)**

**A. Claims 5-8**

Claims 5-8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bass et al. (J. Bacteriology, 178: 1154-61) in view of Loosemore, et al. (1998 Infection and Immunity) and U.S. Pat. No. 5,474,914. The Examiner alleges the references cumulatively teach the instantly claimed invention. Applicants respectfully disagree, as discussed below.

The Examiner alleges that Bass teaches that “the proteolytic activity is not essential to the proteins activity as a chaperone”. The Examiner states:

In actuality, the more effective the protease activity of the protein, the less effective it is as a chaperone. As the reference indicates that the protease activity of the Hin47 inhibits its value as a chaperone, and as the reference does not provide any reason to suspect that this activity is necessary to the proteins secretion from a cell, one of ordinary skill in the art would have had a reasonable expectation that a mutant Hin47 not expressing this proteolytic activity would be a more effective chaperone than the native protein. It is noted that those of skill in the art need only a reasonable expectation of success, not a certainty.

The Examiner correctly states that “certainty” is not required. However, the Federal Circuit has stated that to support an obviousness rejection, a reference must provide a “. . . specific understanding or principle within the knowledge of a skilled artisan that would motivate one with no knowledge of [the] invention to make the combination.” *Beckman Instruments, Inc. v. LKB Produkter AB*, 892 F.2d 1547, 1551, 13 USPQ2d 1301, 1304 (Fed. Cir. 1989). The Examiner cites certain portions of Bass’ disclosure out of context in order to support his conclusions. Bass’ discussion of the function of the E. coli hhoAB genes is reproduced below:

The HtrA/DegP family of proteins are similar to other heat shock proteins in that they help cells adapt to environmental stresses. The classic heat shock (DnaJ, DnaK, GrpE, GroEL, and GroEs in *E. coli*) act as chaperones to aid in the proper folding of proteins. . . . The HtrA/DefP family of proteins may also act as chaperones by binding periplasmic proteins that have just been secreted or those that are denatured under stressful conditions. Either they could release the bound protein toward the proper folding pathway in a chaperone-like mode or the serine protease activity could degrade it. The proteolytic efficiency of the complex would then decide the fate of a protein. In support of this hypothesis, the *Rickettsia* HtrA homolog which lacks the active-site catalytic triad appears to act in a protease-independent manner. The precise role of the HtrA family members in cell growth and pathogenesis remains to be elucidated. (Emphasis added)

One of skill in the art would understand Bass' description of the potential function of the HtrA proteins as conjecture, as opposed to fact. For instance, Bass states that the proteins ". . . may also act as chaperones by binding . . . "; refers to the "proteolytic efficiency" statement as "hypothesis"; and, indicates that the "precise role of the HtrA family members remains to be elucidated". Bass' reference to his position as a "hypothesis" would be understood by one of skill in the art as exactly that: a hypothesis (. . . a tentative assumption . . . insufficient evidence to provide more than a tentative explanation. *Webster's Ninth New Collegiate Dictionary*). In addition, Bass provides no motivation to make the substitutions specifically referred to in the instantly amended claims.

The rejection was made with respect to Bass in view of the 1998 article and Spaete. With respect to the 1998 article, the Examiner states that, without Bass, the 1998 article "appears to provide no motivation to make an expression vector including the leader sequence." (Office Action dated Feb. 25, 2003, p. 14-15). As described above, Applicants believe that Bass provides nothing more than a hypothesis. Applicants respectfully maintain that the 1998 article adds nothing to Bass' tentative assumption.

The Examiner further alleges that Spaete provides the motivation to include a chaperone and a desired protein in the same vector. As stated above, Bass merely provides a hypothesis as to the chaperone activity of HtrA proteins. As suggested above

for the 1998 article, Applicants believe Spaete adds nothing to Bass' tentative assumption.

Applicants respectfully maintain that neither the 1998 article nor Spaete serve to support Bass' hypothesis regarding HtrA function. As such, the combination of Bass with the 1998 article and/or Spaete does not render the instantly claimed invention obvious. Accordingly, Applicants request that the instant rejection be withdrawn.

**B. Claims 9-11**

Claims 9-11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bass, the 1998 article, Spaete, and further in view of Barenkamp and St. Geme III, Molecular Microbiology 19: 1215-23 ("Barenkamp") and U.S. Pat. No. 6,335,182 (the '182 patent). The Examiner alleges the references cumulatively teach the instantly claimed invention. Applicants respectfully traverse this rejection, as discussed below.

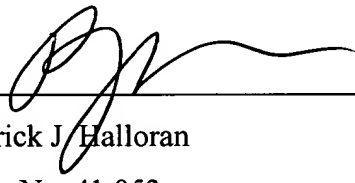
Applicants have addressed the combination of Bass, the 1998 article and Spaete above. As discussed therein, the deficiencies of Bass are not cured by either the 1998 article or Spaete, alone or in combination. Neither Barenkamp nor the '182 patent add anything to Bass' hypothetical suggestions, with or without the other cited references. As such, Applicants respectfully request that this rejection be withdrawn.

**CONCLUSIONS**

Reconsideration of this application is respectfully requested. Applicants believe claims 4-6 and 8-13 are in condition for allowance and request that a Notice of Allowance be issued as soon as possible. The Examiner is encouraged to contact the undersigned to discuss any matter associated with this application.

Respectfully submitted,  
AVENTIS PASTEUR, INC.

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